

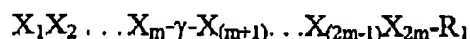
In re application of  
Baird et al  
Application No.: 09/372,474

Atty. Dkt. No. 025098-0701

Amendments to the Claims/Listing of Claims

Please cancel claims 46-49 without prejudice. This listing of claims will replace all **prior** versions, and listings, of claims in the application:

1. (Previously presented) A method for designing a specific polyamide



wherein

$X_1$ ,  $X_2$ ,  $X_m$ ,  $X_{(m+1)}$ ,  $X_{(2m-1)}$ , and  $X_{2m}$  are carboxamide residues forming carboxamide binding pairs  $X_1/X_{2m}$ ,  $X_2/X_{(2m-1)}$ ,  $X_m/X_{(m+1)}$ ;

$\gamma$  is  $\gamma$ -aminobutyric acid or 2,4 diaminobutyric acid, and

$R_1$  is  $-\text{NH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ ,  $-\text{NH}(\text{CH}_2)_{0-12}\text{CONH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ , or  $-\text{NHR}_2$ , where  $R_2$  and  $R_3$  are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl,  $\text{C}_{1-100}$  alkyl,  $\text{C}_{1-100}$  alkylamine,  $\text{C}_{1-100}$  alkyldiamine,  $\text{C}_{1-100}$  alkylcarboxylate,  $\text{C}_{1-100}$  alkenyl, a  $\text{C}_{1-100}$  alkynyl, and  $\text{C}_{1-100}$  alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL- $\alpha$ -lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrinilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, tartaric acid, and (+)- $\alpha$ -tocopheral, suitable for use as a DNA-binding ligand that is selective for identified target DNA-sequences  $5'-\text{WN}_1\text{N}_2 \dots \text{N}_m\text{W}-3'$  where m is an integer having a value from 3 to 6, the method comprising:

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(a) identifying a target sequence of double stranded DNA having the form  $5'-WN_1N_2 \dots N_mW-3'$ ,  $N_1N_2 \dots N_m$  being the sequence to be bound by carboxamide residues, wherein each N is independently chosen from the group A, G, C, and T, each W is independently chosen from the group A and T, and m is an integer having a value from 3 to 6;

(b) representing the identified sequence as  $5'-Wab \dots xW-3'$ , wherein *a* is a first nucleotide to be bound by the  $X_1$  carboxamide residue, *b* is a second nucleotide to be bound by the  $X_2$  carboxamide residue, and *x* is the corresponding nucleotide to be bound by the  $X_m$  carboxamide residue;

(c) defining *a* as A, G, C, or T to correspond to the first nucleotide to be bound by a carboxamide residue in the identified sequence;

(d) selecting Im as the  $X_1$  carboxamide residue and Py as the  $X_{2m}$  carboxamide residue if *a* = G;

(e) selecting Py as the  $X_1$  carboxamide residue and Im as the  $X_{2m}$  carboxamide residue if *a* = C;

(f) selecting Hp as the  $X_1$  carboxamide residue and Py as the  $X_{2m}$  carboxamide residue if *a* = T;

(g) selecting Py as the  $X_1$  carboxamide residue and Hp as the  $X_{2m}$  carboxamide residue if *a* = A; and

(h) repeating steps c – g for *b* through *x* until all carboxamide residues are selected;

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wherein Im is N-methylimidazole, Hp is 3-hydroxy-N-methylpyrrole, Py is N-methylpyrrole, A is adenine, G is guanine, C is cytosine, and T is thymine; and synthesizing the polyamide.

2. (Cancelled)

3. (Previously presented) The method of claim 1 further comprising the step of determining if the binding affinity of the polyamide to the identified target sequence is subnanomolar.

4. (Previously presented) The method of claim 1 further comprising the step of determining if the polyamide exhibits a binding affinity that is at least ten-fold higher for said identified target sequence compared to a non-target DNA sequence.

5. (Previously presented) The method of claim 1 further comprising the step of replacing at least one pyrrole residue with a  $\beta$ -alanine residue.

6-41. (Cancelled)

42. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a regulatory sequence.

43. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a promoter sequence.

44. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a coding sequence.

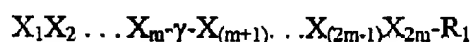
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45. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a non-coding sequence.

46. - 49. (Cancelled)

50. (Previously presented) A method for designing a specific polyamide



wherein

$X_1$ ,  $X_2$ ,  $X_m$ ,  $X_{(m+1)}$ ,  $X_{(2m-1)}$ , and  $X_{2m}$  are carboxamide residues forming carboxamide binding pairs  $X_1/X_{2m}$ ,  $X_2/X_{(2m-1)}$ ,  $X_m/X_{(m+1)}$ , and wherein one carboxamide binding pair is substituted with a  $\beta/\beta$ , wherein  $\beta$  is  $\beta$ -alanine;

$\gamma$  is  $\gamma$ -aminobutyric acid or 2,4 diaminobutyric acid, and

$R_1$  is  $-\text{NH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ ,  $-\text{NH}(\text{CH}_2)_{0-12}\text{CONH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ , or  $-\text{NHR}_2$ , where  $R_2$  and  $R_3$  are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl,  $\text{C}_{1-100}$  alkyl,  $\text{C}_{1-100}$  alkylamine,  $\text{C}_{1-100}$  alkyldiamine,  $\text{C}_{1-100}$  alkylcarboxylate,  $\text{C}_{1-100}$  alkenyl, a  $\text{C}_{1-100}$  alkynyl, and  $\text{C}_{1-100}$  alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL- $\alpha$ -lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrinilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, tartaric acid, and (+)- $\alpha$ -tocopheral, suitable for use as a DNA-binding

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ligand that is selective for identified target DNA-sequences 5'-WN<sub>1</sub>N<sub>2</sub> . . . N<sub>m</sub>W-3' where **m** is an integer having a value from 3 to 6, the method comprising:

(a) identifying a target sequence of double stranded DNA having the form 5'-WN<sub>1</sub>N<sub>2</sub> . . . N<sub>m</sub>W-3', N<sub>1</sub>N<sub>2</sub> . . . N<sub>m</sub> being the sequence to be bound by carboxamide residues, wherein each N is independently chosen from the group A, G, C, and T, each W is independently chosen from the group A and T, and m is an integer having a value from 3 to 6;

(b) representing the identified sequence as 5'-Wab . . . xW-3', wherein *a* is a first nucleotide to be bound by the X<sub>1</sub> carboxamide residue, *b* is a second nucleotide to be bound by the X<sub>2</sub> carboxamide residue, and *x* is the corresponding nucleotide to be bound by the X<sub>m</sub> carboxamide residue;

(c) defining *a* as A, G, C, or T to correspond to the first nucleotide to be bound by a carboxamide residue in the identified sequence;

(d) selecting Im as the X<sub>1</sub> carboxamide residue and Py as the X<sub>2m</sub> carboxamide residue if *a* = G;

(e) selecting Py as the X<sub>1</sub> carboxamide residue and Im as the X<sub>2m</sub> carboxamide residue if *a* = C;

(f) selecting Hp as the X<sub>1</sub> carboxamide residue and Py as the X<sub>2m</sub> carboxamide residue if *a* = T;

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(g) selecting Py as the  $X_1$  carboxamide residue and Hp as the  $X_{2m}$  carboxamide residue if  $a = A$ ; and

(h) repeating steps c – g for  $b$  through  $x$  until all carboxamide residues are selected;

wherein Im is N-methylimidazole, Hp is 3-hydroxy-N-methylpyrrole, Py is N-methylpyrrole, A is adenine, G is guanine, C is cytosine, and T is thymine; and

synthesizing the polyamide.